```
L5   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:648392  CAPLUS Full-text
DN   141:190808
TI   Preparation of aromatic ring-fused cyclic compounds as TGR5 receptor
     agonists
IN   Itoh, Fumio; Hinuma, Shuji; Kanzaki, Naoyuki; Miki, Takashi; Kawamata,
     Yuji; Oi, Satoru; Tawaraishi, Taisuke; Ishichi, Yuji; Hirohashi, Mariko
PA   Takeda Chemical Industries, Ltd., Japan
SO   PCT Int. Appl., 337 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
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PI   WO 2004067008        A1    20040812   WO 2004-JP706          20040127
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
     JP 2004346059        A2    20041209   JP 2004-18643          20040127
PRAI JP 2003-19272        A     20030128
     JP 2003-124311       A     20030428
OS   MARPAT 141:190808
GI
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I

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AB    It is intended to provide G protein-coupled receptor (TGR5) agonists
      containing fused ring compds. represented by the following general formula
      (I), salts or prodrugs thereof (wherein the ring A represents an optionally
      substituted aromatic ring; and the ring B represents a 5- to 8-membered ring
      having one or more substituents).  Also disclosed are regulators for physiol.
      functions involving TGR5, preventives and/or remedies for various diseases
      involving TGR5, cytokine production inhibitors, GLP-1 secretion promoters,
      insulin secretion promoters, appetite depressants, pancreas regenerants,
      promoters for pancreas β-cell differentiation or proliferation, insulin
      resistance improvers, or immunosuppressants. containing the compds. I.  In
      particular disclosed are preventives and/or remedies containing the compds. I
      for heart failure, myocardial infarction, acute kidney failure, angina
      pectoris, arrhythmia, bronchial asthma, chronic obstructive pulmonary disease,
      arteriosclerosis, chronic articular rheumatism, diabetes, obesity, insulin
      secretion failure, pancreas fatigue, gastric ulcer, ulcerative colitis,
      allergy, osteoarthritis, erythematodes, or excessive immune reaction after
      transplant surgery.  The compds. I are also useful for screening ligands,
      agonists, or antagonists of TGR5.  Thus, 0.1 g 2-[trans-7-chloro-5-(3-
      formylphenyl)-1-neopentyl-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]- N-
      (2-fluorobenzyl)acetamide was reduced by NaBH4 in MeOH at room temperature for
      30 min to give 76 mg 2-[trans-7-chloro-5-(3-hydroxyphenyl)-1-neopentyl-2- oxo-
      1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]-N-(2-fluorobenzyl)acetamide (II).
      II at 1 μM increased the production of cAMP in CHO cells expressing human TGR5
      by 128%.  Pharmaceutical formulations containing specific compound I were also
      prepared
IT   737785-65-8P 737785-66-9P 737785-67-0P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
```
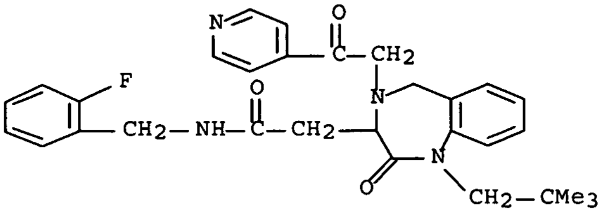

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of aromatic ring-fused cyclic compds. as TGR5 receptor agonists, cytokine production inhibitors and appetite depressants)

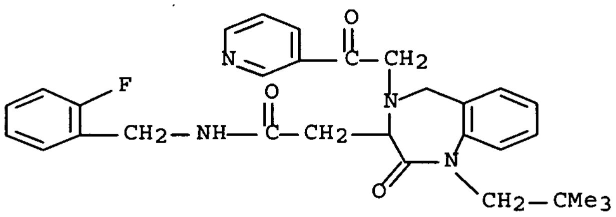
RN 737785-65-8 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 1-(2,2-dimethylpropyl)-N-[(2-fluorophenyl)methyl]-2,3,4,5-tetrahydro-2-oxo-4-[2-oxo-2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



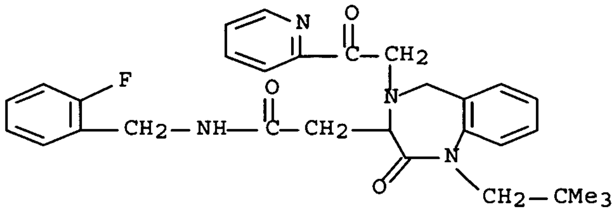
RN 737785-66-9 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 1-(2,2-dimethylpropyl)-N-[(2-fluorophenyl)methyl]-2,3,4,5-tetrahydro-2-oxo-4-[2-oxo-2-(3-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 737785-67-0 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 1-(2,2-dimethylpropyl)-N-[(2-fluorophenyl)methyl]-2,3,4,5-tetrahydro-2-oxo-4-[2-oxo-2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



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L5   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:333703  CAPLUS Full-text
DN   140:339346
TI   Preparation of sulfonylbenzodiazepinoneacetamides as bradykinin
     antagonists
IN   Holcomb, Rayan C.; Grant, Francine S.; Pleiss, Michael A.; Thorsett,
     Eugene D.
PA   Elian Pharmaceuticals Inc, USA
SO   PCT Int. Appl., 105 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.             KIND    DATE        APPLICATION NO.         DATE
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PI   WO 2004033436           A1     20040422    WO 2003-US32389         20031009
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             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW:  GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004138208           A1     20040715    US 2003-685353          20031009
PRAI US 2002-417165P         P      20021010
OS   MARPAT 140:339346
GI
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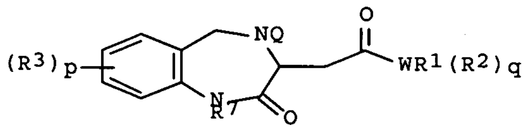

I

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AB   Title compds. [I; Q = SO2R, CH2COR; W = O, S, N; R = (substituted) aryl,
     heteroaryl, heterocyclyl; R1, R2 = H, (substituted) alkyl, alkenyl, alkynyl,
     aryl, cycloalkyl, heteroaryl, heterocyclyl; R1R2N = (substituted) heteroaryl,
     heterocyclyl; R3 = (substituted) alkyl, alkenyl, alkynyl, amino, cycloalkyl,
     alkoxy, aryl, aryloxy, heteroaryl, heterocyclyl, heterocyclyloxy, acyl,
     acyloxy, halo, NO2, cyano, OH, etc.; ≥2 R3 = atoms to form (substituted)
     cycloalkyl, aryl, heteroaryl, heterocyclyl rings; p = 0-3; q = 0, 1], were
     prepared  Thus, [2-(tert-butoxycarbonyl)-4- oxo-2,5-benzodiazepin-3-yl]-N-[2-
     (pyridin-4-yl)ethyl]acetamide (preparation given) was heated in HCO2H at 40°
     for 2 h to give a residue which was stirred with 4-chloro-2,5-
     dimethylbenzenesulfonyl chloride in pyridine at room temperature overnight to
     give [2-(4-chloro-2,5-dimethylbenzenesulfonyl)- 4-oxo-2,5-benzodiazepin-3-yl]-
     N-[2-(pyridin-4-yl)ethyl]acetamide.  I showed bradykinin B1 receptor agonist
     activity in the range of IC50 = 0.1-10,000 nM.
IT   680972-87-6P 680972-88-7P 680972-89-8P
     680972-90-1P 680972-91-2P 680972-94-5P
     680972-95-6P 680972-96-7P 680972-97-8P
     680972-98-9P 680972-99-0P 680973-00-6P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)(claimed compound; preparation of sulfonylbenzodiazepinoneacetamides as
     bradykinin antagonists)
RN   680972-87-6  CAPLUS
CN   1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-
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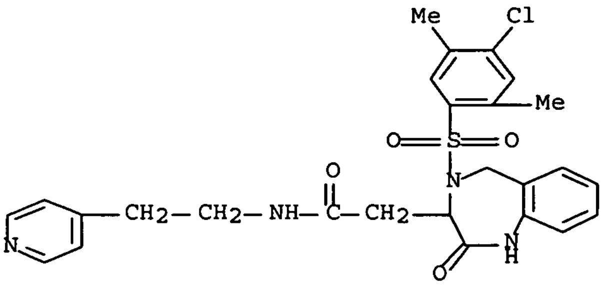
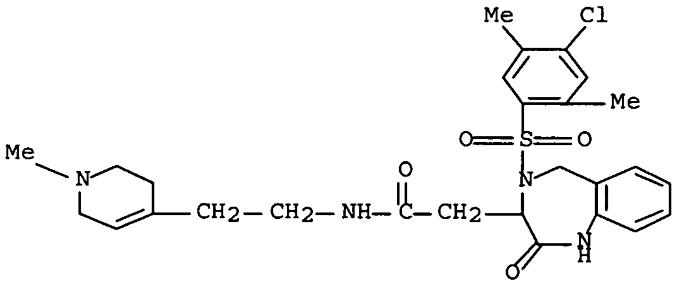
dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



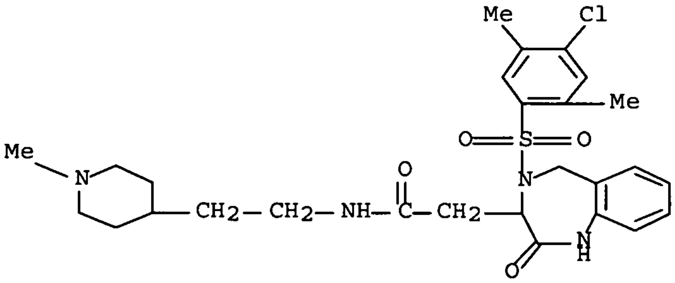
RN 680972-88-7 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-(1,2,3,6-tetrahydro-1-methyl-4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



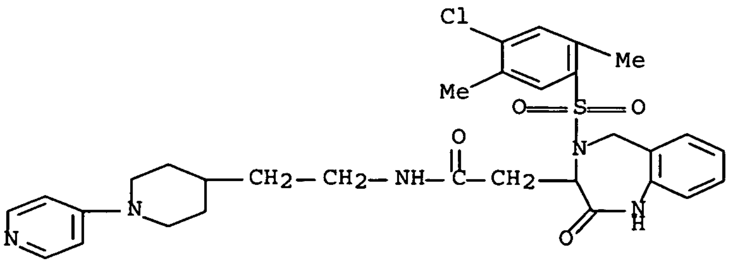
RN 680972-89-8 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-N-[2-(1-methyl-4-piperidinyl)ethyl]-2-oxo- (9CI) (CA INDEX NAME)



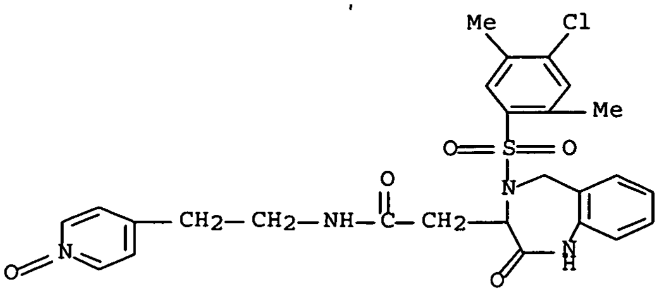
RN 680972-90-1 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-[1-(4-pyridinyl)-4-piperidinyl]ethyl]- (9CI) (CA INDEX NAME)



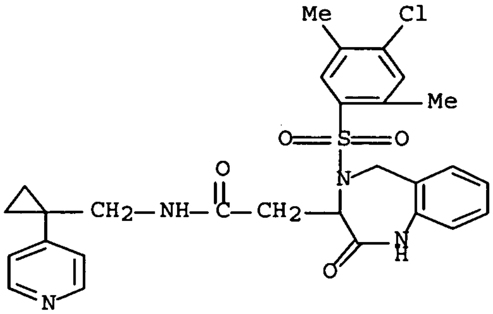
RN 680972-91-2 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-N-[2-(1-oxido-4-pyridinyl)ethyl]-2-oxo- (9CI) (CA INDEX NAME)



RN 680972-94-5 CAPLUS

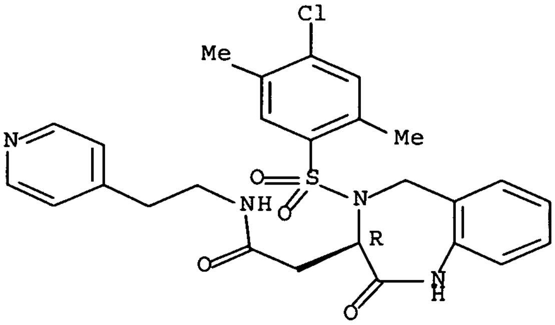
CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[[1-(4-pyridinyl)cyclopropyl]methyl]- (9CI) (CA INDEX NAME)



RN 680972-95-6 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-(4-pyridinyl)ethyl]-, (3R)- (9CI) (CA INDEX NAME)

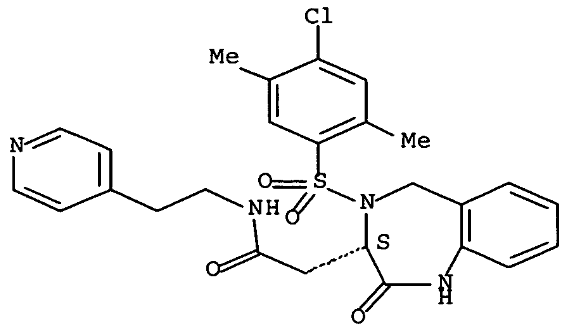
Absolute stereochemistry.



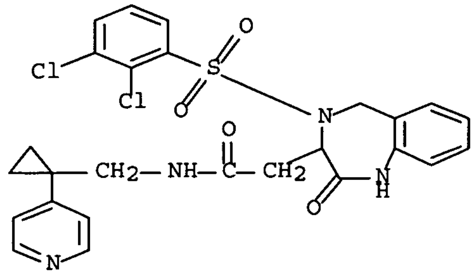
RN 680972-96-7 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-(4-pyridinyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

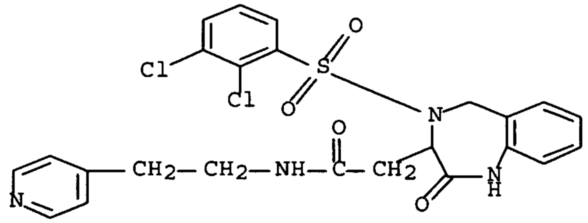
Absolute stereochemistry.



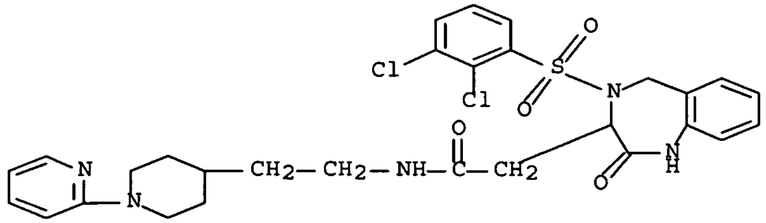
RN 680972-97-8 CAPLUS
CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(2,3-dichlorophenyl)sulfonyl]-
2,3,4,5-tetrahydro-2-oxo-N-[[1-(4-pyridinyl)cyclopropyl]methyl]- (9CI)
(CA INDEX NAME)



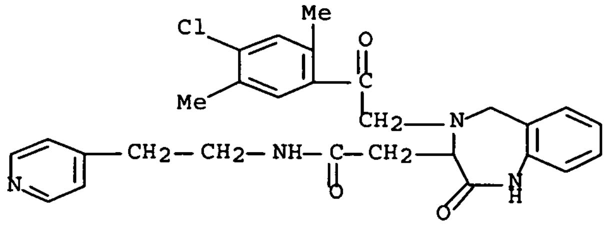
RN 680972-98-9 CAPLUS
CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(2,3-dichlorophenyl)sulfonyl]-
2,3,4,5-tetrahydro-2-oxo-N-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 680972-99-0 CAPLUS
CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(2,3-dichlorophenyl)sulfonyl]-
2,3,4,5-tetrahydro-2-oxo-N-[2-[1-(2-pyridinyl)-4-piperidinyl]ethyl]- (9CI)
(CA INDEX NAME)



RN 680973-00-6 CAPLUS
CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[2-(4-chloro-2,5-dimethylphenyl)-2-
oxoethyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-(4-pyridinyl)ethyl]- (9CI) (CA
INDEX NAME)



IT 680973-09-5P 680973-10-8P 680973-12-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of sulfonylbenzodiazepinoneacetamides as bradykinin antagonists)

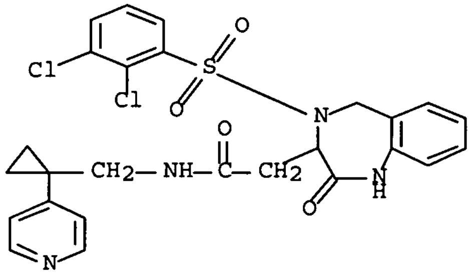
RN 680973-09-5 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(2,3-dichlorophenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[[1-(4-pyridinyl)cyclopropyl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 680972-97-8

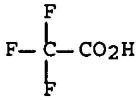
CMF C26 H24 Cl2 N4 O4 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



F_3C-CO_2H

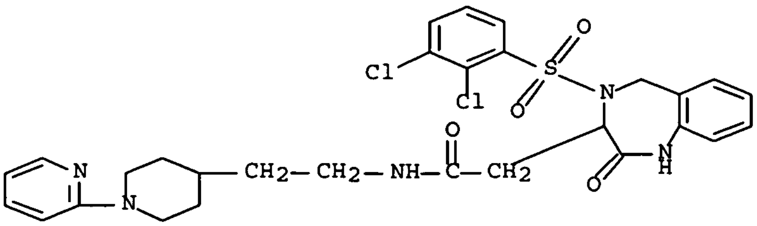
RN 680973-10-8 CAPLUS

CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(2,3-dichlorophenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-[1-(2-pyridinyl)-4-piperidinyl]ethyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

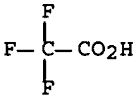
CRN 680972-99-0

CMF C29 H31 Cl2 N5 O4 S

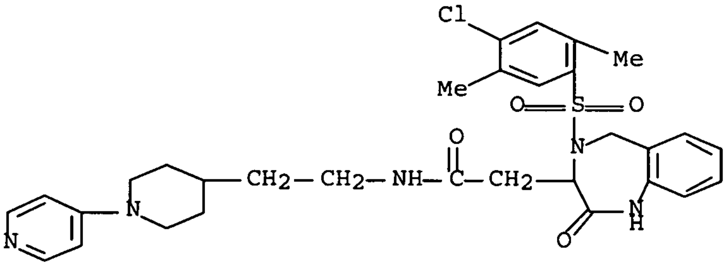


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 680973-12-0 CAPLUS
CN 1H-1,4-Benzodiazepine-3-acetamide, 4-[(4-chloro-2,5-dimethylphenyl)sulfonyl]-2,3,4,5-tetrahydro-2-oxo-N-[2-[1-(4-pyridinyl)-4-piperidinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L10  ANSWER 1 OF 1  MARPAT  COPYRIGHT 2005 ACS on STN
AN   124:176161  MARPAT Full-text
TI   Preparation of 1,4-benzodiazepin-2-one-1-acetamides as cholecystokinin-A
     receptor agonists
IN   Aquino, Christopher Joseph; Dezube, Milana; Sugg, Elizabeth Ellen;
     Sherrill, Ronald George; Willson, Timothy Mark; Szewczyk, Jerzy Ryszard
PA   Glaxo Wellcome Inc., USA
SO   PCT Int. Appl., 121 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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PI   WO 9528399         A1   19951026      WO 1995-EP1335   19950413
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             MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,
             TM, TT
         RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
             SN, TD, TG
     AU 9524462         A1   19951110      AU 1995-24462    19950413
     EP 755394          A1   19970129      EP 1995-918554   19950413
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
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     ZA 9503111         A    19960123      ZA 1995-3111     19950418
     US 5795887         A    19980818      US 1996-718552   19961011
PRAI GB 1994-7468       19940415
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     GB 1994-20702      19941014
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GI
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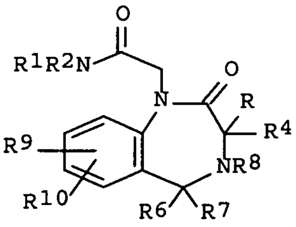
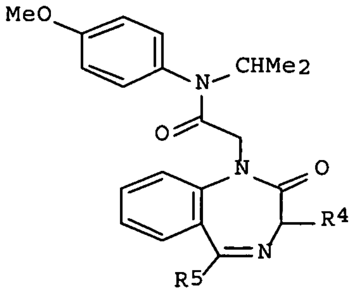


I



II

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AB    Title compds. [I; R = (CH2)n(NH)p(CO)q(NH)rR3; R1 = (cyclo)alkyl,
      (un)substituted Ph; R2 = (cyclo)alkyl, (un)substituted Ph, alkenyl, etc.;
      NR1R2 = tetrahydroquinolyl, substituted benzazepinyl; R3 = H, = (cyclo)alkyl,
      (un)substituted Ph, heteroaryl, etc.; R4 = H, alkyl, alkoxy, etc.; R6 =
      (CH2)mR5; R5 = H, = (cyclo)alkyl, (un)substituted Ph, -heteroaryl, etc.; R7 =
      H; R6R7 = O; R8 = H, (un)substituted alkyl, NH2, CO2H, etc.; R7R8 = bond;
      R9,R10 = H or halo; m,n = 0-3; p,q,r, = 0 or 1] were prepared  Thus, 3-
      benzyloxycarbonylamino-5-(3-pyridyl)-1,3- dihydrobenzo[e][1,4]diazepin-2-one
      was N-alkylated by BrCH2CON(CHMe2)C6H4(OMe)-4 (preparation given) and the
      deprotected product condensed with PhNCO to give title compound II (R4 =
      NHCONHPh, R5 = 3-pyridyl).  II (R4 = 1H-indazol-3-ylmethyl, R5 = 2-
      pyridyl)(preparation not given) gave 100% inhibition of guinea pig gall
      bladder segment contraction at 30µM in vitro and 2.5% rat gastric emptying at
      0.1mol/kg i.p.
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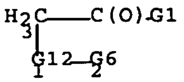
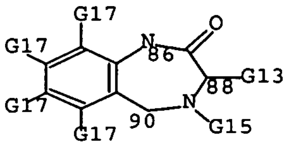
MSTR 1

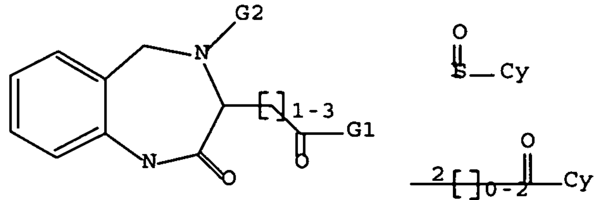


G13 = alkyl<(1-3)> (SR CO2H)
G18 = 86-3 88-2 90-145



G26 = S(O)
G27 = Ph
DER: or pharmaceutically acceptable acid addition or organic base addition salts
MPL: claim 1
NTE: substitution is restricted

```
=> d l2; d his; log y
L2 HAS NO ANSWERS
L1                STR
```



```
 G1 O,S,N
 G2 [@1],[@2]

Structure attributes must be viewed using STN Express query preparation.
L2                QUE  ABB=ON  PLU=ON  L1

     (FILE 'REGISTRY' ENTERED AT 18:11:17 ON 09 JUN 2005)
                  DEL HIS Y
L1                STRUCTURE UPLOADED
L2                QUE L1
L3              0 S L2
L4             18 S L2 FUL

     FILE 'CAPLUS' ENTERED AT 18:12:43 ON 09 JUN 2005
L5              2 S L4

     FILE 'BEILSTEIN' ENTERED AT 18:13:19 ON 09 JUN 2005
L6              0 S L2
L7              0 S L2 FUL

     FILE 'MARPAT' ENTERED AT 18:13:44 ON 09 JUN 2005
L8              0 S L2
L9              3 S L2 FUL
L10             1 S L9 NOT L5


COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                      118.15     290.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)           SINCE FILE      TOTAL
                                                          ENTRY    SESSION
CA SUBSCRIBER PRICE                                       -0.68      -2.14

STN INTERNATIONAL LOGOFF AT 18:14:27 ON 09 JUN 2005
```